Claims 3-4 - Examiner rejects these claims based on "obvious-type double patenting". However, as stated by the examiner on p1-6 and top of p7, it is not possible to use a predict a therapeutic activity (in fungi, restenosis etc.). Similarly it is not possible to predict a drug's mechanism of action based on similar derivative's activity. IAABE was not published prior to Dec 1999 and therefore predictions of its mechanism of action cannot be made based on the mechanism of action of BAABE reported in Feb 1999 in 6,294,695. The Novel Mechanisms are clearly pointed out in Neoplasia 1 (6) p.498-507 and they are part of the basis for the present application. This is contrary to the statement made on p7 of the recent Office Action (5 lines up from the bottom) that the activities of the compound structure described in USP 6,294,695 are inherent in them. Obviously this cannot be true of IAABE because that would be based on a prediction. The prediction being M-phase arrest (based on BAABE) which is not the case for IAABE which causes a G1/S arrest. We request that these claims remain in the application.

Claims 3-4 – Examiner rejects these claims based on 35 USC $112 as being indefinite. These claims can be re-worded as such:

We request that Claim 3 is deleted and the following Claims added to replace it:

NEW Claim 8: A tubulin ligand that causes a G1/S-phase arrest.

NEW Claim 9: The medicinal drug of Claim1 wherein it causes tumor volume reduction of prostate cancer in a model organism.

NEW Claim 10: The medicinal drug of Claim1 wherein it cures prostate cancer in 20% of cases in a model organism.

NEW Claim 11: The medicinal drug of Claim1 wherein it causes selective cell death of T-cell Leukemia cancer cells.

NEW Claim 12: The medicinal drug of Claim1 wherein it causes selective cell death of Myelodisplasia syndromes cell types.

NEW Claim 13: The medicinal drug of Claim1 wherein it causes selective cell death of Melanoma cells.

NEW Claim 14: The medicinal drug of Claim1 wherein it has anti-cancer activity.

NEW Claim 15: The medicinal drug of Claim1 wherein it causes selective cell death of Renal Cancer cells.

NEW Claim 16: The medicinal drug of Claim1 wherein it causes selective cell death of Breast Cancer cells.

NEW Claim 17: The medicinal drug of Claim1 wherein it causes selective cell death of Non-small Cell Lung Cancer cells.

NEW Claim 18: The medicinal drug of Claim1 wherein it causes selective cell death of Colon Cancer cells.

NEW Claim 19: The medicinal drug of Claim1 wherein it causes selective cell death of lymphoma wild type cancer cells.

NEW Claim 20: The medicinal drug of Claim1 wherein it causes selective cell death of lymphoma MDR negative cancer cells.

NEW Claim 21: The medicinal drug of Claim1 wherein it does not cause cell death of normal lymphocytes when added to a culture of these cells at the ID90 dose of lymphoma.

Claim 4 can be re-worded as follows:

We request Claim 4 be re-worded as follows:

Claim 4 – A tubulin ligand that causes a biphasic phosphorylation of bcl-2, one phase being between 1-3h and the next phase being 12h onwards.

NEW Claim 22 – A situation where the 1-3h Bcl2 phosphorylation phase could be used as a tool to develop anti-cancer drugs with similar or improved potency.

Office Action p10 – 35 USC $102a. Claim 3 is rejected (5-7 are already deleted) based on being anticipated. Considering "anticipation" is defined as "deal with or use before due time" this is clearly not the case in Jiang et al 1998 because IAABU is not the same as IAABE. Also this statement falls under the "prediction" argument (see above), where the mechanism of bcl2 phosphorylation could not and was not predicted before this present application, as it is a Unique mechanism of action. From above "As stated by the examiner on p1-6 and top of p7, it is not possible to use a predict a therapeutic activity (in fungi, restenosis etc.). Similarly it is not possible to predict a drug's mechanism of action based on similar derivative's activity. IAABE was not published prior to Dec 1999 and therefore predictions of its mechanism of action cannot be made based on the mechanism of action of BAABE reported in Feb 1999 in 6,294,695. The Novel Mechanisms are clearly pointed out in Neoplasia 1 (6) p.498-507 and they are part of the basis for the present application. This is contrary to the statement made on p7 of the recent Office Action (5 lines up from the bottom) that the activities of the compound structure described in USP 6,294,695 are inherent in them. Obviously this cannot be true of IAABE because that would be based on a prediction."

We request that Claim 3 remain in the application.

Office Action p10 last line and half of p11: 35 USC $103 - Obviousness. It is not clear what this section is referring to specifically.

Office Action lower half of p11 plus p12,13,14,15. 35 USC $103 – Obviousness ? . With all due respect, the Examiner's remarks are not in line with the current understanding in the cell cycle field. The cell cycle is a well established phenomena that operates differently than a mechanically linked system. Where the Examiner is trying to relate the cell cycle to a rigid mechanism the premise is incorrect. An analogy for a rigid mechanism is a clock's gearing system, if one cog is forcefully stopped then all other cogs will be stopped. However, an analogy for the Cell Cycle is an automatic transmission in a car, in this case if the brakes are put on, the engine will not stop so it is not rigid. The Cell Cycle is not a rigid system in this sense and so stopping (or arresting) at M-phase will not stop or eliminate G1, S or G2 phases. The Cell Cycle will pass through these Phases and the cells will accumulate in M-phase. This is referred to by Dr. MA Jordan who was reference on p14 of Office Action (see attached e-mail correspondence). Dr. Jordan was asked for feedback concerning the Examiner's remarks, her reply is evidence of the flexible nature of the Cell Cycle as described above.

In addition, it must be added that a population of cells are not synchronized, in fact they are a mixture of all Phases of the Cell Cycle. So a drug is not added just before M-phase in order to arrest in M-phase, a drug is added to a population of cells and they begin to accumulate in M-phase when they reach that Phase, having passed through the other phases. This is another example of the "flexible" nature of the cell cycle as compared to a rigid mechanical mechanism.

In this instance it is clear there is a basic misunderstanding of the cell cycle which hopefully is now rectified. In the case of this application the fact that a Tubulin ligand arrests cells in G1/S phase is a unique mechanism of action (prior to this finding all known tubulin ligands caused M-phase arrest in cancer cells) and therefore we wish to keep Claim 4 in this application.

Amended list of Claims is attached to this letter.

We hope this clarifies our perspective on these issues, we understand that it is not possible for the Examiners to be equally knowledgeable of all areas of science, and our remarks are made respectfully and with this understanding. We are looking forward to future correspondence with a view to getting our first patent approved.

Yours sincerely,

Ashley Davis,

Cytoskeleton Inc.

Amended Claims

Claim 1 [Deleted mistakenly] One novel compound: Iodine acetamido benzoyl ethyl acetate.

Claim 2. [Deleted mistakenly] Halogenated acetamido benzoyl ethyl acetate derivatives that covalently bind to tubulin.

Claim 3. [Delete and add modifications Claims 8-21] Tubulin ligands with a G1/S-phase arrest mechanism of anti-cancer activity.

Claim 4. [Modified see below New Claim 4 and NEW Claim 22] Tubulin ligands that cause a rapid and biphasic phosphorylation of bcl-2.

5. [Delete] In combination with claims 1 through 4 and bromine acetamido benzoyl ethyl acetate: Compounds that have therapeutic potential in cancer treatment.

6. [Delete] In combination with claims 1 through 4 and bromine acetamido benzoyl ethyl acetate: Compounds that may have therapeutic potential in treating other diseases such as fungal and parasitic infections or malaria.

7. [Delete] In combination with claims 1 through 4 and bromine acetamido benzoyl ethyl acetate: Compounds that may have therapeutic potential in treating other indications such as gout, restenosis, multiple sclerosis, Parkinsons's and Alzheimer's diseases.

We request that Claim 3 is deleted and the following Claims added to replace it:

NEW Claim 8: A tubulin ligand that causes a G1/S-phase arrest.

NEW Claim 9: The medicinal drug of Claim1 wherein it causes tumor volume reduction of prostate cancer in a model organism.

NEW Claim 10: The medicinal drug of Claim1 wherein it cures prostate cancer in 20% of cases in a model organism.

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NEW Claim 18: The medicinal drug of Claim1 wherein it causes selective cell death of Colon Cancer cells.

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Amended Claim 4 – A tubulin ligand that causes a biphasic phosphorylation of bcl-2, one phase being between 1-3h and the next phase being 12h onwards.

NEW Claim 22 – A situation where the 1-3h Bcl2 phosphorylation phase could be used as a tool to develop anti-cancer drugs with similar or improved potency.

New Claim 23 One novel compound: Iodine acetamido benzoyl ethyl acetate.

New Claim 24. Halogenated acetamido benzoyl ethyl acetate derivatives that covalently bind to tubulin.